Martin, T. C. S., Rauch, A., Salazar-Vizcaya, L., & Martin, N. (2018). Understanding and Addressing Hepatitis C Virus Reinfection Among Men Who Have Sex with Men. *Infectious Disease Clinics of North America*, *32*(2), 395-405. https://doi.org/10.1016/j.idc.2018.02.004

Title: Understanding and addressing HCV reinfection among men who have sex with men

Authors: Thomas CS Martin[1], Andri Rauch[2], Luisa Salazar-Vizcaya[2], Natasha K Martin[1,3],

Affiliations:
[1]Division of Infectious Diseases and Global Public Health, University of California San Diego.
[2]Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
[3]School of Social and Community Medicine, University of Bristol.

[§]**Corresponding author:** Natasha Martin, Division of Global Public Health, 9500 Gillman Drive MC 0507, La Jolla, California, 92093. Natasha-martin@ucsd.edu +1(858)822-4802.

Word Count: 2928

Figures: 1
Tables: 1

Funding Acknowledgements. NKM is supported by the National Institute for Drug Abuse [grant number R01 DA037773-01A1] and the University of California San Diego Center for AIDS Research (CFAR), a National Institute of Health (NIH) funded program [grant number P30 AI036214] which is supported by the following NIH Institutes and Centers: NIAID, NCI, NIMH, NIDA, NICHD, NHLBI, NIA NIGMS, and NIDDK. The views expressed are those of the authors and not necessarily those of the National Institutes of Health.

Disclosures: TM has no disclosures. NM has received unrestricted research grants from Gilead unrelated to this work and honoraria from Merck, Gilead, and AbbVie. AR reports support to his institution for advisory boards and/or travel grants from Janssen-Cilag, MSD, Gilead Sciences, Abbvie, and Bristol-Myers Squibb, and an unrestricted research grant from Gilead Sciences. All remuneration went to his home institution and not to AR personally, and all remuneration was provided outside the submitted work.

Key words: hepatitis c virus, reinfection, prevention, men who have sex with men

Key points/Summary:

- HCV reinfection incidence rates among HIV-infected men who have sex with men (MSM) range from 3-15 per 100 person-years. These rates are 3-10 times higher than baseline incidence.
- As settings strive to meet the World Health Organization elimination targets, concerns surround the high reinfection in this population. Modeling indicates that tackling increasing incidence and high reinfection requires widespread HCV treatment combined with behavioral interventions.
- Behavioral interventions studies addressing HCV reinfection are required, such as the ongoing *HCVree* trial in Switzerland targeting MSM who engage in inconsistent condom use.
- Other interventions may include traditional harm reduction interventions, adapted behavioral interventions targeting HIV risks among substance using populations, and interventions to prevent risk related to substance use with sex.

Introduction

Among people living with HIV worldwide, it has been estimated that 2.4% (IQR 0.8 – 5.8) are coinfected with hepatitis C virus (HCV), yet this rises to 6.4% (IQR 3.2 – 10.0) among men who have sex with men (MSM)[1]. Indeed, an epidemic of HCV among HIV-infected (HIV+) men who have sex with men (MSM) has been documented in major urban centers in the United States, Europe, and Australia, with dramatic increases in HCV incidence and/or prevalence in the past decade[2-10]. This epidemic has been associated not only with injection drug use (IDU), but also with high-risk sexual practices and substance use with sex among those with no history of IDU[11]. As HIV+ individuals are living longer in the era of highly active antiretoriviral therapies, the morbidity and mortality associated with viral hepatitis coinfection increases. Consequently, liver-related mortality is one of the leading non-AIDS causes of death among HIV+ individuals[12].

The World Health Organization recently released targets for HBV and HCV elimination, which included a 90% relative reduction in new infections and a 65% relative reduction in hepatitis-related mortality by 2030[13]. As a result, policymakers are looking for evidence-based preventions strategies to achieve these targets. Recent advanced in HCV direct-acting antiviral therapies (DAAs) have resulted in short-term (8-12 week), all-oral, highly tolerable treatments with cure rates in excess of 90% for both HCV moninfected and HIV/HCV coinfected individuals alike[14]. This has led to substantial optimism that expansion of HCV treatment could both lead to individual cure and also potential prevention of onwards transmission[15].

However, due to the high cost of HCV therapy, concerns regarding reinfection continue to hamper efforts to scale-up HCV treatment for those at risk of transmission such as MSM and people who inject drugs.

In this paper we discuss the empirical evidence surrounding HCV reinfection among MSM, modeling evidence of the importance of reinfection on achieving HCV elimination, and potential strategies to reduce reinfection.

HCV reinfection among MSM: epidemiological evidence

Reinfection with HCV following treatment or spontaneous clearance has been demonstrated in animal models, people who inject drugs and more recently among HIV+ MSM[16]. Indeed, several studies in the pre-DAA era have demonstrated that the reinfection incidence among HIV+ MSM in Western Europe and the U.S. is alarmingly high - approximately 3-10 times the baseline incidence in this population[17-20]. A summary of studies of reinfection incidence rates following successful treatment is shown in **Figure 1**.

The first of these studies, performed in Amsterdam, retrospectively identified 56 HIV+ MSM who had been successfully treated for acute HCV between 2003 and 2011 [18]. There were 11 confirmed reinfections using phylogenetic analysis of the E2/HVR region of the virus, yielding a reinfection incidence of 15.2 per 100 person-years (/100py) (95% CI 8.0-26.5). This reinfection incidence was approximately 10 times the primary HCV infection incidence among HIV+ MSM in Amsterdam [21]. The authors also found that for individuals who had behavioral data, those that underwent reinfection were

more likely to report non-injecting recreational drug use than those that did not undergo reinfection.

In London, a retrospective cohort study from 2004-2012 examined HCV reinfection incidence following both successful treatment and spontaneous clearance of HCV infection [19]. Among 191 patients who were either treated for HCV infection or who spontaneously cleared their infection, 44 reinfections occurred, representing an incidence of 7.8/100py (95%CI 5.8-10.5). This reinfection rate is 6-7 times the observed primary incidence among HIV+ MSM in the UK (1.02-1.38 per 100py) [22]. Interestingly the authors found indication of a higher reinfection rate among those treated for HCV (9.6/100py, 95%CI 6.6-14.1) than among those who spontaneously cleared their infection (4.2/100py, 95%CI 1.7-10) though the difference did not reach significance. The authors hypothesized that this may be due to a degree of protective immunity developed among individuals who spontaneously clear their infection making it less likely they become reinfected or that if any reinfection occurred it was spontaneously cleared.

In a larger multicenter study between 2002-2014 including eight hospitals across Austria, France, Germany and the UK from the European AIDS Treatment Network (NEAT), nearly a third of HIV+ MSM were reinfected with HCV within 5 years of clearing their primary infection either through successful treatment or spontaneous clearance [17]. Among 606 HIV+ MSM who cleared their primary infections, 143 were reinfected, with an overall reinfection incidence of 7.3/100py (95%CI 6.2-8.6) [17]. The reinfection

incidence per center is shown in **Table 1**. As in the London study, a trend for lower reinfection incidence following spontaneous clearance of the initial HCV infection when compared to those that were successfully treated was observed (HR 0.62, 95%CI 0.38-1.02, p=0.06). Individuals who spontaneously cleared their initial infection were more likely to spontaneously clear any reinfection, supporting the possibility of protective immunity or favorable host defenses such as the IL28B CC genotype. The authors additionally found that the incidence of a second reinfection (18.8/100py, 95%CI 12.9-27.5) was higher compared to the incidence of first reinfection (HR 2.5, 95%CI 1.7-3.8), suggesting that the HCV epidemic may in part be being driven by a small group of high-risk individuals.

Outside Europe but still during the pre-DAA era, one recent retrospective study in San Diego, California found that among 43 HIV+ MSM who had been successfully treated for their HCV infection between 2008 and 2015, 3 became reinfected yielding a reinfection incidence of 2.9/100py (95% CI 0.6-8.4) [20]. This compared to a local primary incidence of 1.2/100py (95%CI 1.0-1.4), indicating that reinfection rates may be 2-3 fold that of primary infection.

The studies discussed above were performed in the period that prolonged interferon containing regimens were the standard of care. Given the shorter courses and much greater tolerability of DAA therapy, concerns have arisen that improved therapy may lead to an increase in risk taking behavior and higher reinfection incidence. One study to date has examined HCV reinfection in the DAA era. This was an analysis of the German hepatitis C cohort

(GECCO) looking at HCV reinfection following DAA therapy between 2014-2016, finding that among 175 HIV+ MSM treated between February 2014 and May 2016, 7.4% (13/175) were reinfected [23]. Further work examining reinfection incidence rates in the DAA era will shed important light on this issue.

No studies have identified behavioral risks specifically associated with HCV reinfection among HIV+MSM. However, numerous studies have explored risk behaviors associated with HCV prevalence and incidence in this population, showing that fisting[24-28], rectal trauma with bleeding[28], condomless receptive anal intercourse (AI)[24, 29, 30], group sex[24, 28, 29], injecting drug use (IDU)[25, 29], sex while high on methamphetamine [30], consumption of gamma hydroxbutyrate (GHB)[25], recreational use of cocaine, ecstasy, GHB, ketamine, amphetamine, or methamphetamine before or during sexual contact[27] are associated with HCV acquisition. Interventions aimed at reducing risk of HCV infection/reinfection should therefore target these associated risks.

Modeling the impact of reinfection on achieving HCV elimination among PWID versus MSM populations

A number of theoretical epidemic modeling studies have evaluated the potential impact of scaled-up of HCV prevention on HCV prevalence and incidence among people who inject drugs, including the risk of reinfection. Empirical studies have shown that HCV reinfection rates among PWID are low (3% per year in the IFN-containing era)[31]. Unfortunately few studies have directly compared HCV primary incidence and reinfection rates among PWID

in the same setting, but the reported rates are broadly similar to, if not lower than primary incidence rates. As a conservative assumption, the vast majority of epidemic models have assumed that the risk of reinfection is equal to primary infection, and have studied settings with varied incidence from 3%-30% per year, in North America, Europe, Asia, and Australia[32-36]. In general, these studies have found that despite the risk of reinfection, HCV incidence and prevalence can be dramatically reduced (in many settings by 90% by 2030) with scaled-up HCV treatment to rates to below 100 per 1000 PWID annually, particularly in combination with harm reduction. As such, relatively modest levels of treatment are required to eliminate HCV despite this risk of reinfection.

Despite this encouraging evidence, a few recent epidemic modeling analyses have shown that achieving substantial reductions in HCV incidence among HIV+ MSM populations is likely to be more challenging compared to among PWID due to relatively high rates of existing HCV treatment combined with elevated risk of reinfection (indicating a high risk core group) and increasing incidence over time in many settings such as Switzerland and Berlin [37-39]. Existing modeling studies have focused on the UK, Switzerland, Berlin, and the Netherlands, showing that achieving >80% reduction in incidence requires treating virtually all MSM upon diagnosis combined with risk reduction to prevent infection/reinfection. In the UK, a modeling study indicated that scaled-up rates of DAA therapy (from 46% to 80% treated within a year of diagnosis and from 7%/year to 20%/year thereafter) could reduce incidence among HIV+ MSM over 60% by 2030, but could not meet elimination

targets[37], thus likely requiring additional behavioral interventions. Similar modeling findings in Switzerland prompted the generation of a behavioral intervention among MSM, described below.

The Swiss HCVree behavioral intervention trial and epidemic modeling

Since the mid 2000's, an outbreak of incident HCV infections among HIV+ MSM became evident in Switzerland [10, 40]. This new epidemic co-occurred with a rise in self-reported condomless sex with occasional partners in this population [10]. Men who have sex with men accounted for 24% and 85% of all incident HCV infections in the Swiss HIV Cohort Study (SHCS, www.shcs.ch) before and after 2006 respectively [41]. The health care system responded with a 10-fold increase in HCV treatment rate [10, 38]. Rising treatment rates coincided with increased awareness of this epidemic and the advent of better treatments, namely DAA [42]. But such increases in treatment rate did not result in reduced HCV incidence among HIV+ MSM. Due to the high costs of these drugs [43], reimbursement in Switzerland was initially restricted to people who had reached advanced stages of liber fibrosis. This inhibited early treatment of incident infections with DAAs outside clinical trials.

Treatment reimbursement restrictions were however not the only barrier to tackle the rising epidemic. A model of HCV transmission among HIV+ MSM was developed and calibrated to Switzerland and projected the effect of treatment interventions assuming different scenarios of risk behavior. The model suggested that high rates of DAA-based treatment may fail at reducing

HCV primary and reinfection incidence if sexual practices associated with transmission continue to rise among the MSM population, but could lead to declining incidence if the frequency of such practices stabilizes. Moreover, the model projected that in 2030 57% of all infections would be reinfections if risk behavior rises and 23% if risk behavior stabilizes [38].

Given these projections and the limitations imposed by regulatory reimbursement restrictions, clinicians from the SHCS engaged in a 1-year clinical trial that provided early treatment for HCV infections in MSM and prevented reinfections through risk counselling. The study includes three phases: First, all MSM were screened for replicating HCV infection with HCV RNA; second, all participants infected with HCV genotypes 1 or 4 were offered treatment with grazoprevir/elbasvir ±ribavirin; and third, HCV RNA screening will be repeated in all MSM to assess the effect of this intervention on HCV prevalence. The study started in October 2015 with the screening of 4 257 MSM [44]. One hundred and seventy eight (4.8%) had a replicating HCV infection. Of those, 94% were infected with HCV genotypes 1 or 4 and were offered treatment with the study drugs. The evaluation of the treatment phase and the subsequent re-screening phase is currently ongoing. In addition to HCV treatment, enrolled patients who reported inconsistent condom use with occasional partners received four 45-minute sessions of individual sexual risk counseling at weeks 4, 6, 8, and 12. This behavioral intervention which was specifically developed for this patient group included detailed interviews and computer-assisted counselling similar to a previous European Multi-center study targeting HIV positive MSM [45].

Salazar-Vizcaya et al. subsequently used epidemic modeling to predict the potential impact of the *Swiss HCVree trial* in order to assess the potential of this type of (short-term) treatment plus *intensive intervention* counseling. Simulations considered *intensive intervention* and hypothetical scenarios of treatment and risk behavior simultaneously. The model suggested that *intensive intervention* would considerably reduce incidence over the intervention period, but if after *intensive intervention* treatment was deferred in line with reimbursement regulations, this benefit would dissipate in the long-term. Interestingly, even though high treatment rates after *intensive intervention* led to nearly the same simulated prevalence with or without *intensive intervention* in the long-term, *intensive intervention* was predicted to save treatment costs [46]. As a consequence of the model projections, the *HCVree trial* was extended until the end of 2017. New incident infections as well as reinfections will be treated during this period.

Additionally, reimbursement regulations for DAA-based HCV therapy changed in May 2017, and DAA therapy is now reimbursed irrespective of fibrosis stage in all HIV+ patients. We therefore expect trends in risk behavior to shape the future course of HCV transmission among HIV+ MSM in Switzerland, making behavioral interventions such as the *Swiss HCVree* trial even more critical.

Other interventions to prevent infection/reinfection among MSM:

In addition to behavioral interventions addressing inconsistent condom use

among MSM at risk for HCV infection/reinfection (such as the Swiss *HCVree trial*), effective behavioral interventions targeting other HCV-related risks among MSM are urgently required.

Traditional harm reduction interventions targeting MSM who inject drugs: There is mounting evidence that traditional harm reduction interventions such as opiate substitution therapy (OST) and high coverage needle and syringe programs (NSP) are effective at reducing HCV transmission among people who inject drugs. A recent Cochrane review and meta-analysis found that OST reduce the risk of acquiring HCV by 50% (RR=0.50, 95% CI: 0.40-0.63) [47]. In addition, high NSP coverage was found to reduce HCV acquisition by 23% (RR=0.77, 95% CI: 0.38-1.54) [47], with higher impact seen in Europe (RR=0.44, 95% CI: 0.24-0.80) [47]. When combining high coverage of both NSP and OST interventions, the risk of acquiring HCV was reduced by an estimated 71% (RR=0.29, 95% CI: 0.13-0.65) [47]. Despite this evidence, the impact of harm reduction among MSM who inject drugs has not been studied specifically. Additionally, MSM who inject drugs may not self-identify as people who inject drugs, and therefore may not access traditional harm reduction services.

Adapted HIV prevention interventions among MSM: It is unclear whether interventions to prevent HIV transmission among MSM would be effective to prevent HCV infection among MSM. However, given potential shared transmission routes it is possible these interventions could be used or adapted. There is an extensive body of literature on behavioral interventions

to reduce unprotected anal intercourse and HIV transmission among MSM[48]. For example, a Cochrane review and meta-analysis of 40 behavioral interventions found a reduction of occasions of or partners for unprotected anal sex by 27% (95%CI 15%-37%) compared to no or minimal intervention[48]. One intervention, *Project ECHO*, targets substance using MSM and uses Personalized Cognitive Counseling to help participants identify and avoid risky sexual and drug using behaviors[49]. Among HIV-negative MSM who reported sex after substance use in the past 6 months, Project ECHO reduced the number of condomless anal intercourse events with non-primary partners by 46% (RR = 0.56; 95% CI 0.34 - 0.92) compared to the control group[49]. Studies exploring whether interventions similar to or adapted from *Project ECHO* are effective for HCV prevention among MSM are warranted.

Chemsex intervention: There is an emerging body of literature examining the development of educational and counseling interventions targeted at MSM who use crystal methamphetamine with sex ("ChemSex") [50-52], which may reduce the risk of acquiring HCV among this population. ChemSex is associated with HCV infection, as well as high risk behaviors such as multiple sexual partners, transactional sex, group sex, fisting, sharing sex toys, injecting drug use, higher alcohol consumption and the use of 'bareback' sexual networking applications[53].

In one HIV/GUM clinic in London, following completion of HCV treatment, clinicians provide MSM with harm reduction messages, education on HCV transmission risks related to ChemSex, ChemSex packs including safe

injecting equipment and educational information and referal to on-site, ChemSex behaviour change support [52]. It has been reported that ChemSex motivations are often associated with internalized homophobia and shame surrounding homosexual sex, gay cultural/societal norms, sexual performance anxieties, and body image concerns. Successful behavioral interventions for MSM at risk of acquiring/transmitting HCV in ChemSex environments would need to address these sensitive issues.

Conclusion

HCV reinfection rates among MSM are high (3-15 per 100 person-years), and are 3-10 fold higher than rates of primary incidence, indicating a high-risk core group of MSM at risk for HCV infection and reinfection. Factors associated with HCV infection among MSM point towards a number of varied sexual and drug-related risks, which could be targeted for interventions to prevent infection/reinfection. Modeling indicates that tackling increasing incidence and high reinfection rates requires high levels of HCV treatment combined with behavioral interventions. Enhanced testing strategies and prompt retreating of reinfection may be required to promptly diagnosed reinfections and prevent further onwards transmissions. Others have suggested strategies such as home-based dried blot spot collection at fixed time points or after a risk event. Behavioral interventions studies addressing HCV reinfection are required, such as the *HCVree* trial in Switzerland. Other relevant interventions may include traditional harm reduction interventions targeting MSM who inject drugs, adapted behavioral interventions targeting HIV risks among substance using populations, and interventions to prevent harms related to chemsex and

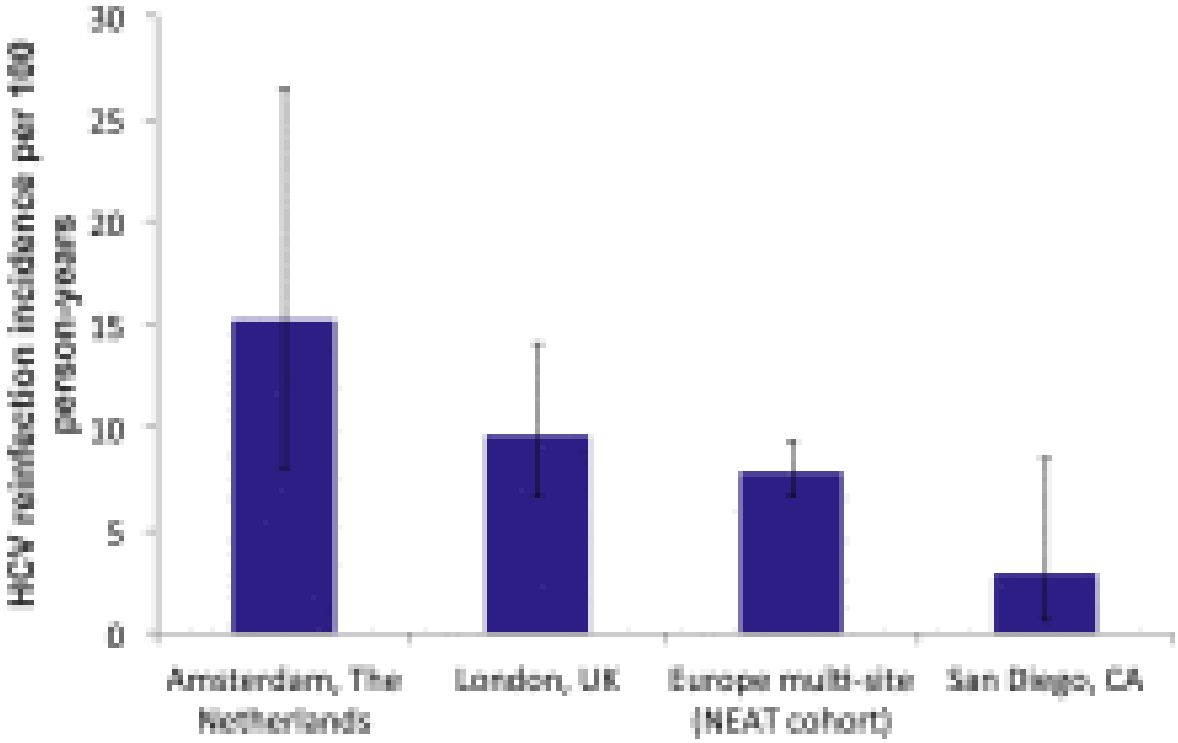
other risk associated with drug use with or before sexual episodes. It is likely that a suite of interventions targeting different sub-subpopulations and risks among MSM will be required, instead of one blanket intervention.

Centre	Incidence reinfections/100py (95% CI)	Number of reinfections	Person years follow up
Dusseldorf (n=59)	8.1 (4.6-14.3)	12	148
Hamburg (n=73)	5.0 (2.9-8.7)	13	258
Berlin (n=95)	8.2 (5.6-12.1)	26	316
Bonn (n=11)	4.8 (0.7-33.7)	1	21
London – Chelwest (n=190)	7.0 (5.3-9.1)	52	746
London – Royal Free (n=69)	5.7 (3.7-8.7)	21	369
Paris (n=27)	21.8 (11.3-41.8)	9	41
Vienna (n=28)	16.8 (8.7-32.3)	9	54

Table 1. HCV reinfection incidence among HIV+ MSM in Europe. From Ingilitz et al.[17].

FIGURE LEGENDS

FIGURE 1. HCV reinfection incidence after successful treatment among HIV+ MSM as reported in Amsterdam, London, the NEAT cohort, and San Diego, California [17-20].



Reference

1. **Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. *The Lancet Infectious Diseases.* 16(7):797-808.**
2. **Yaphe S, Bozinoff N, Kyle R, Shivkumar S, Pai NP, Klein M. Incidence of acute hepatitis C virus infection among men who have sex with men with and without HIV infection: a systematic review. *Sexually transmitted infections.* Nov 2012;88(7):558-564.**
3. **Bradshaw D, Matthews G, Danta M. Sexually transmitted hepatitis C infection: the new epidemic in MSM? *Current opinion in infectious diseases.* Feb 2013;26(1):66-72.**
4. **Danta M, Brown D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. *AIDS (London, England).* May 11 2007;21(8):983-991.**
5. **van de Laar TJ, Matthews GV, Prins M, Danta M. Acute hepatitis C in HIV-infected men who have sex with men: an emerging sexually transmitted infection. *AIDS (London, England).* Jul 31 2010;24(12):1799-1812.**
6. **Hagan H, Jordan AE, Neurer J, Cleland CM. Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. *AIDS (London, England).* Nov 2015;29(17):2335-2345.**
7. **Jordan AE, Perlman DC, Neurer J, Smith DJ, Des Jarlais DC, Hagan H. Prevalence of hepatitis C virus infection among HIV+ men who have sex with men: a systematic review and meta-analysis. *International journal of STD & AIDS.* Jan 28 2016.**
8. **van der Helm JJ, Prins M, del Amo J, et al. The hepatitis C epidemic among HIV-positive MSM: incidence estimates from 1990 to 2007. *AIDS (London, England).* May 15 2011;25(8):1083-1091.**
9. **Urbanus AT, van de Laar TJ, Stolte IG, et al. Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. *AIDS (London, England).* Jul 31 2009;23(12):F1-7.**
10. **Wandeler G, Gsponer T, Bregenzer A, et al. Hepatitis C virus infections in the Swiss HIV Cohort Study: a rapidly evolving epidemic. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Nov 15 2012;55(10):1408-1416.**
11. **Sexual transmission of hepatitis C virus among HIV-infected men who have sex with men--New York City, 2005-2010. *MMWR. Morbidity and mortality weekly report.* Jul 22 2011;60(28):945-950.**
12. **Smith CJ, Ryom L, Weber R, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. *The Lancet.* 384(9939):241-248.**

13. World Health Organization. Global Health Sector Strategy on Viral Hepatitis, 2016-2021. 2016.
14. Wyles DL, Sulkowski MS, Dieterich D. Management of Hepatitis C/HIV Coinfection in the Era of Highly Effective Hepatitis C Virus Direct-Acting Antiviral Therapy. *Clinical Infectious Diseases.* 2016;63(suppl_1):S3-S11.
15. Martin NK, Vickerman P, Grebely J, et al. Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. *Hepatology.* 2013;58(5):1598-1609.
16. Grebely J, Prins M, Hellard M, et al. Hepatitis C virus clearance, reinfection, and persistence, with insights from studies of injecting drug users: towards a vaccine. *The Lancet infectious diseases.* 2012;12(5):408-414.
17. Ingiliz P, Martin TC, Rodger A, et al. HCV reinfection incidence and spontaneous clearance rates in HIV-positive men who have sex with men in Western Europe. *Journal of hepatology.* Feb 2017;66(2):282-287.
18. Lambers FA, Prins M, Thomas X, et al. Alarming incidence of hepatitis C virus re-infection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM. *AIDS (London, England).* Nov 13 2011;25(17):F21-27.
19. Martin TC, Martin NK, Hickman M, et al. Hepatitis C virus reinfection incidence and treatment outcome among HIV-positive MSM. *AIDS (London, England).* Oct 23 2013;27(16):2551-2557.
20. Chaillon A, Anderson C, Martin T, et al. Incidence of Hepatitis C Among HIV-infected Men Who Have Sex With Men, 2000-2015. *Conference on Retroviruses and Opporunistic Infections (CROI)*. Seattle, USA2017.
21. Vanhommerig J, Stolte IG, Lambers FA, et al. Hepatitis C Virus Incidence in the Amsterdam Cohort Study among Men who have Sex with Men: 1984-2011. *Conference*2014.
22. Martin NK, Thornton A, Hickman M, et al. Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America.* 02/16
10/14/received
02/05/accepted 2016;62(9):1072-1080.
23. Ingiliz P, Christensen S, Berger F, et al. HCV REINFECTION AFTER SUCCESSFUL DAA TREATMENT: A GECCO ANALYSIS. *Conference on Retroviruses and Opportunistic Infections (CROI) 2015. Seattle, Washington. Feb 13-16 2017. Abstract 567.*
24. Danta M, Brown D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. *AIDS (London, England).* 2007;21:983-991.

25. Urbanus A, van de Laar T, Stolte I, et al. Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. *AIDS (London, England).* 2009;23(12):F1-7.
26. Turner JM, Rider AT, Imrie J, et al. Behavioural predictors of subsequent hepatitis C diagnosis in a UK clinic sample of HIV positive men who have sex with men. *Sexually transmitted infections.* August 1, 2006 2006;82(4):298-300.
27. Matser A, Vanhommerig J, Schim van der Loeff MF, et al. HIV-Infected Men Who Have Sex with Men Who Identify Themselves as Belonging to Subcultures Are at Increased Risk for Hepatitis C Infection. *PLoS ONE.* 03/04
10/02/received
01/24/accepted 2013;8(3):e57740.
28. Schmidt AJ, Rockstroh JK, Vogel M, et al. Trouble with Bleeding: Risk Factors for Acute Hepatitis C among HIV-Positive Gay Men from Germany—A Case-Control Study. *PLoS ONE.* 03/08
10/01/received
02/10/accepted 2011;6(3):e17781.
29. Witt M, Seaberg EC, Darilay A, et al. Incident Hepatitis C Virus Infection in Men Who Have Sex With Men: A Prospective Cohort Analysis, 1984-2011. *Clin Infec Dis.* 2013;57(1):77-84.
30. Fierer D, Factor S, Uriel A, et al. Sexual Transmission of Hepatitis C Virus Among HIV-infected Men Who Have Sex with Men - New York City 2005-2010. *Morbidity and Mortaility Weekly Report.* 2011;60(28):945-950.
31. Simmons B, Saleem J, Hill A, Riley RD, Cooke GS. Risk of Late Relapse or Reinfection With Hepatitis C Virus After Achieving a Sustained Virological Response: A Systematic Review and Meta-analysis. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America.* 01/19
07/30/received
10/30/accepted 2016;62(6):683-694.
32. Scott N, McBryde ES, Thompson A, Doyle JS, Hellard ME. Treatment scale-up to achieve global HCV incidence and mortality elimination targets: a cost-effectiveness model. *Gut.* April 12, 2016 2016.
33. Martin N, Hickman M, Hutchinson S, Goldberg D, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modelling the impact of antiviral treatment, needle and syringe programmes, and opiate substitution therapy. *Clin Infec Dis.* 2013;57(suppl 2):S39-S45.
34. Gountas I, Sypsa V, Anagnostou O, et al. Treatment and primary prevention in people who inject drugs for chronic hepatitis C infection: Is elimination possible in a high prevalence setting? *Addiction.* 2017;doi: 10.1111/add.13764. [Epub ahead of print].
35. Cousien A, Tran VC, Deuffic-Burban S, Jauffret-Roustide M, Dhersin J-S, Yazdanpanah Y. Hepatitis C Treatment as Prevention of Viral Transmission and Liver-related Morbidity in Persons Who Inject Drugs. *Hepatology.* 2015;(in press) DOI: 10.1002/hep.28227.

36. Lima VD, Rozada I, Grebely J, et al. Are Interferon-Free Direct-Acting Antivirals for the Treatment of HCV Enough to Control the Epidemic among People Who Inject Drugs? *PLOS ONE.* 2015;10(12):e0143836.
37. Martin NK, Thornton A, Hickman M, et al. Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights. *Clinical Infectious Diseases.* 2016;62(9):1072-1080.
38. Salazar-Vizcaya L, Kouyos RD, Zahnd C, et al. Hepatitis C virus transmission among human immunodeficiency virus-infected men who have sex with men: Modeling the effect of behavioral and treatment interventions. *Hepatology.* 2016;64(6):1856-1869.
39. Hullegie S, Nichols B, Rijnders B, et al. Is HCV Elimination Possible? A Modeling Study of HIV-Positive MSM. *Conference on Retroviruses and Opportunistic Infections (CROI) 2016, Boston, Massachusetts Feb 22-25 2016.*;Abstract #536.
40. Rauch A, Martin M, Weber R, et al. Unsafe Sex and Increased Incidence of Hepatitis C Virus Infection among HIV-Infected Men Who Have Sex with Men: The Swiss HIV Cohort Study. *Clinical Infectious Diseases.* 2005;41(3):395-402.
41. Wandeler G, Schlauri M, Jaquier M-E, et al. Incident Hepatitis C Virus Infections in the Swiss HIV Cohort Study: Changes in Treatment Uptake and Outcomes Between 1991 and 2013. *Open Forum Infectious Diseases.* 02/19
11/03/received
02/12/accepted 2015;2(1):ofv026.
42. Béguelin C, Suter A, Bernasconi E, et al. Trends in HCV treatment uptake, efficacy and impact on liver fibrosis in the Swiss HIV Cohort Study. *Liver International.*n/a-n/a.
43. Iyengar S, Tay-Teo K, Vogler S, et al. Prices, Costs, and Affordability of New Medicines for Hepatitis C in 30 Countries: An Economic Analysis. *PLoS Medicine.* 05/31
10/19/received
04/18/accepted 2016;13(5):e1002032.
44. Braun DL, Kouyos RD, Hampel BH, et al. Systematic HCV-RNA Screen in HIV+ MSM Reveals High Numbers of Potential Transmitters. *Conference on Retroviruses and Opportunistic Infections (CROI)*. Boston, USA2017.
45. Nöstlinger C, Platteau T, Bogner J, et al. Implementation and Operational Research: Computer-Assisted Intervention for Safer Sex in HIV-Positive Men Having Sex With Men: Findings of a European Randomized Multi-Center Trial. *Journal of Acquired Immune Deficiency Syndromes (1999).* 02/10
05/14/received
10/14/accepted 2016;71(3):e63-e72.
46. Salazar-Vizcaya L, Kouyos RD, Fehr J, et al. On the potential of a short-term intensive intervention to interrupt HCV transmission in HIV-positive men who have sex with men: A mathematical modelling study. *Journal of Viral Hepatitis.*n/a-n/a.

47. **Platt L, Reed J, Minozzi S, et al. Effectiveness of needle/syringe programmes and opiate substitution therapy in preventing HCV transmission among people who inject drugs. *Cochrane Database Syst Rev.* 2016;2016(1).**
48. **Johnson W, Diaz R, Flanders W, et al. Behavioral interventions to reduce risk for sexual transmission of HIV among men who have sex with men. *Cochrane Database of Systematic Reviews.* 2008(3):Art. No.: CD001230. DOI: 001210.001002/14651858.CD14001230.pub14651852.**
49. **Coffin PO, Santos G-M, Colfax G, et al. Adapted Personalized Cognitive Counseling for Episodic Substance-Using Men Who Have Sex with Men: A Randomized Controlled Trial. *AIDS and behavior.* 2014;18(7):1390-1400.**
50. **Pakianathan MR, Lee MJ, Kelly B, Hegazi A. How to assess gay, bisexual and other men who have sex with men for chemsex. *Sexually transmitted infections.* 2016;92(8):568-570.**
51. **Stuart D, Weymann J. ChemSex and care-planning: One year in practice. *HIV Nursing.* 2015;15:24-28.**
52. **Stuart D. Sexualised drug use by MSM (ChemSex): a toolkit for GUM/HIV staff. *HIV Nursing* 2014;14(2):15.**
53. **Hegazi A, Lee M, Whittaker W, et al. Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men attending sexual health clinics. *International journal of STD & AIDS.* 2017;28(4):362-366.**